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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	21

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/020,716	Applicant(s) Rudolf Jung, et al.
	Examiner Amy Nelson	Group Art Unit 1638

X Responsive to communication(s) filed on *Jul 31, 2000* .

X This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

X Claim(s) *57-74* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

X Claim(s) *57-74* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Sequence Rules

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

Specifically, Applicant has not identified in the specification all of the sequences in the Sequence Listing. Applicant's amendment to the specification filed 7/31/00 requested deletion of the paragraph which identified the sequences of SEQ ID NO:8-22. The amendment incorrectly stated that the paragraph was at page 59 of the specification. However, page 59 of the specification is the abstract. It is believed that Applicant intended deletion of the paragraph at page 40 of the specification. Hence, the appropriate paragraph at page 40 has been deleted. As a consequence of the deletion, the sequences of SEQ ID NO:8-22 are no longer identified in the specification. Appropriate correction is required.

It is noted that the sequences of SEQ ID NO:14-22 were introduced in the Sequence Listing filed 3/15/00. Applicant indicated that the sequences did not constitute new matter, and indicated that support for the sequences could be found at pages 12 and 13 of the specification. Applicant should amend pages 12 and 13 of the specification to indicate how each of the sequences of SEQ ID NO:14-22 are supported by the cited references.

Furthermore, the sequences on page 28 of the specification are not identified by SEQ ID NO.

Full compliance with the Sequence Rules is required in response to this Official action. A complete response to this Official action should include both compliance with the Sequence Rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set forth in this Official action will be held to be non-responsive.

Claim Rejections - 35 USC § 112

2. Claims 57-74 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is repeated for the reasons of record set forth in the Official actions mailed 5/18/99, 11/22/99, and 4/21/00. Applicant's arguments filed 7/31/00 have been fully considered but they are not persuasive.

Applicant asserts that other modified or unmodified genes are disclosed in the specification and/or were known in the art at the time of Applicant's invention, which could have been substituted for the modified hordothionin gene of SEQ ID NO:2. Therefore, Applicant has provided an adequate written description to support the claimed invention (response, p. 5-6). Examiner responds that the amended claims are directed to methods for increasing methionine and lysine in plant seed, to plants and seeds produced by said methods, and to expression cassettes for use in said methods. It is not clear that any of the genes described in the instant specfication encodes a protein with increased methionine and lysine content, and therefore could be substituted for the modified hordothionin gene

in the claimed methods. Most, if not all, of the described genes encode either methionine-rich proteins or sulfur-rich (*i.e.* methionine and cysteine-rich) proteins. Hence, it is not clear from the instant specification that Applicant was in possession of the invention as broadly claimed.

3. Claims 57-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to transformed cereal plant seed having an elevated lysine, methionine and cysteine content (about 10% to about 35% by weight compared to untransformed cereal plant seed) comprising the modified hordothionin gene of SEQ ID NO:2 (HT12), vectors, plant cells and transformed plants comprising said modified hordothionin gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims. This rejection is repeated for the reasons of record set forth in the Official actions mailed 5/18/99 11/22/99, and 4/21/00. Applicant's arguments filed 7/31/00 have been fully considered but they are not persuasive.

Applicant asserts that the instant specification teaches methods for preparation of expression cassettes comprising an endosperm-preferred promoter operably linked to a nucleotide sequence encoding a high lysine and high methionine protein, amino acid analysis of seeds, and separation of embryo and endosperm tissue. Therefore, Applicant asserts that the instantly claimed invention is enabled by the specification (response, p. 6-7). Examiner responds that Applicant has only taught a single nucleotide sequence which encodes a protein which is both high in lysine and high in methionine, namely the modified hordothionin gene. It is not clear that any or all of the other claimed

genes encode proteins which are modified in both amino acids. Moreover, Applicant has not provided guidance for production of transgenic plants, and particularly transgenic seed which comprise increased methionine and lysine levels in their endosperm other than by transformation with the disclosed modified hordothionin gene of SEQ ID NO:2. If, as Applicant asserts, the instant invention is novel over the Falco reference because Falco was unsuccessful in obtaining increased lysine in the endosperm, presumably due to higher lysine catabolism in the endosperm, then the claims of the instant invention should be limited in scope to the teachings of unexpected results. Because Applicant has provided guidance for only a single gene which could be successfully expressed in endosperm resulting in increased lysine and methionine levels, the claimed invention should be so limited.

Re: Claim 59. Applicant has not provided guidance for specific expression in the endosperm other than by targeting with an endosperm-preferred promoter. Therefore, the claims should be so limited. The claim should be amended to specifically recite transformation with an endosperm-preferred promoter.

4. Claims 57-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At Claim 57, "a cereal plant seed" (singular) at line 1 is inconsistent with "transformed seeds" (plural) at line 6. Appropriate correction is required.

At Claim 57, line 2, before "plant cell" --cereal-- should be inserted to agree with the preamble of the claim.

At Claim 57, line 5, "the transformed plant cell" lacks proper antecedent basis.

At Claim 57, line 6, after "transformed seeds" --from the transformed plant-- should be inserted for clarity.

At Claim 59, line 2, "the seed endosperm" lacks proper antecedent basis and should be changed to --the endosperm--.

At Claim 59, line 3, and Claims 69-71, line 2, "an endosperm" should be changed to --the endosperm-- because a seed has only a single endosperm.

At Claim 74, "a cereal plant seed" (singular) at line 1 is inconsistent with "transformed seeds" (plural) at line 10. Appropriate correction is required.

At Claim 74, line 2, before "plant cell" --cereal-- should be inserted to agree with the preamble of the claim.

At Claim 74, lines 4-8, the phrase "polynucleotide comprises ... albumin" is indefinite because all of the alternatives are proteins, and it is unclear how a polynucleotide can comprise a protein. Appropriate correction is required.

At Claim 74, line 6, "Seq ID No. 16" should be changed to the standard format of --SEQ ID NO:16--.

At Claim 74, line 7, "Seq ID No. 18" should be changed to the standard format of --SEQ ID NO:18--.

At Claim 74, line 9, "the transformed cell" lacks proper antecedent basis.

At Claim 74, line 10, after "transformed seeds" --from the transformed plant-- should be inserted for clarity.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 65-68 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims encompass untransformed cells and seeds which are products of nature, and not one of the five statutory statutory classes of patentable subject matter. Amendment of the claims to recite --transformed-- would obviate this rejection.

Claim Rejections - 35 USC § 103

7. Claims 57-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falco *et al.* (U.S. Patent 5,773,691) in view of Applicant's Admission.

In view of Applicant's amendments to the claims, this rejection has been changed to an obviousness rejection. Although Falco does not teach transformation methods to increase lysine and methionine, nor transgenic plants and seeds with enhanced lysine and methionine, it would have been obvious to modify the invention of Falco to also express a gene encoding a methionine-rich protein,

in order to obtain seeds with increased lysine and methionine. Genes encoding methionine-rich proteins were known in the art, as admitted by Applicant (specification, p. 12-13), and it was known in the art that threonine, methionine and lysine were essential amino acids missing from crop plants and required for animal nutrition.

Applicant asserts that because Falco does not teach both increased methionine and lysine, Falco does not anticipate the claimed invention (response, p. 8). In view of the claim amendments, the rejection over the Falco reference has been changed to an obviousness rejection.

8. Claims 57-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rao *et al.* (U.S. Patent 5,885,802) and Rao *et al.* (U.S. Patent 5,990,389) in view of Applicant's Admission. This rejection is repeated for the reasons of record as set forth in the last Official action mailed 4/21/00. Applicant's arguments filed 7/31/00 have been fully considered but they are not persuasive.

This rejection has been modified to remove the previously cited Rao reference (U.S. Patent 5,885,801), directed to modified threonine levels, because the amended claims are limited to plants, seeds, and methods with increased methionine and lysine content. Also, the rejection is modified to reflect that the invention is obvious over Rao ('802) and Rao ('389) because it would have been obvious to combine the teachings of Rao ('802) and Rao ('389) to produce plants that are both methionine-rich and lysine-rich.

Applicant asserts that the claimed invention is distinguished from Rao by the use of an endosperm-specific promoter, and a gene encoding a methionine-rich and lysine-rich protein, and

there is no suggestion to combine references (response, p. 8-9). Examiner responds that because Rao ('802) teaches plant transformation with a mutant hordothionin gene encoding a methionine-rich protein, and Rao ('389) teaches plant transformation with a mutant hordothionin gene encoding a lysine-rich protein, it would have been obvious to combine the teachings of Rao ('802) and Rao ('389) to obtain plants which are increased in both lysine and methionine. It futher would have been obvious to modify the invention of Rao ('802) and Rao ('389) to direct expression of the mutant genes to the endosperm by expressing them behind an endosperm-specific promoter as admitted by Applicant to have been well known in the art. Hordothionine is a seed protein and hence expression in the seed (the major portion of which is endosperm) would be expected to be successful. Also, it was well known in the art that increased nutritional value of seeds was particularly desirable given the importance of grains as a food source in the impoverished regions of the world. One would have had a reasonable expectation of success in view of the success of both Rao ('802) and Rao ('389). In view of the broad scope of the claims, it is submitted that the invention is still obvious in view of the prior art references. If, as Applicant asserts, unexpected results were achieved with the instantly disclosed modified hordothionin gene, then the scope of the claimed invention should be limited to the teachings of unexpected results.

9. Claims 57-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jaynes *et al.* (U.S. Patent 5,811,654) in view of Applicant's Admission. This rejection is repeated for the reasons

of record as set forth in the last Official action mailed 4/21/00. Applicant's arguments filed 7/31/00 have been fully considered but they are not persuasive.

Applicant asserts that Jaynes teaches away from using an endosperm-preferred promoter by teaching use of the CaMV 35S promoter or the CaMV 19S promoter. Also, Applicant asserts that Falco teaches away from using an endosperm-prefered promoter by teaching that lysine catabolism is expected to be much greater in the endosperm (response, p. 9-10). Examiner responds that, as stated previously, it was well known in the art that increased nutritional value of seeds (the major portion of which is endosperm tissue) was particularly desirable given the importance of grains as a food source in the impoverished regions of the world. Hence, it would have been obvious to substitute an endosperm-preferred promoter, as admitted by Applicant to have been known in the art, for the CaMV 35S or CaMV 19S promoters disclosed by Jaynes. If, as Applicant asserts, Falco teaches away from using an endosperm-preferred promoter, then the teachings of the instant specification constitute unexpected results, and the scope of the claimed invention should be commensurate with the teachings of unexpected results. Because Applicant has only provided guidance for a single modified hordothionin gene, the claimed invention should be so limited.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy J. Nelson whose telephone number is (703) 306-3218. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310. The fax phone number for this Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application, or if the examiner cannot be reached as indicated above, should be directed to the Group receptionist whose telephone number is (703) 308-1234.

Amy Nelson

AMY J. NELSON, PH.D
PRIMARY EXAMINER

Amy J. Nelson, Ph.D.
August 8, 2000